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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/598,810	09/12/2006	Adrian Brown	PU60746	1607

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GlaxoSmithKline
GLOBAL PATENTS -US, UW2220
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EXAMINER	
SHEIKH, HUMERA N	

ART UNIT	PAPER NUMBER
1615	

NOTIFICATION DATE	DELIVERY MODE
02/03/2011	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

US_cipkop@gsk.com

Office Action Summary	Application No.	Applicant(s)	
	10/598,810	BROWN ET AL.	
	Examiner	Art Unit	
	Humera N. Sheikh	1615	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *18 November 2010*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *47-85* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *47-85* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *7/23/10; 11/18/10*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Status of the Application

Receipt is acknowledged of the Response to Non-Final Office Action, the Amendment and Terminal Disclaimer, all filed 11/18/10 and the Information Disclosure Statements (IDS) filed 07/23/10 and 11/18/10.

Applicant has overcome the following objection(s) and/or rejection(s) by virtue of the amendment to the claims and/or persuasive remarks: (1) The claim objections for claims 63 and 84 have been withdrawn and (2) The provisional nonstatutory obviousness-type double patenting rejections over copending Application No. 10/470,438 and copending Application No. 10/470,439 have been withdrawn.

Claims 47-85 are pending in this action. New claim 85 has been added herein. Claims 53, 54, 63, 65-68, 77, 78 and 84 have been amended. Claims 1-46 have previously been cancelled. Claims 47-85 remain rejected.

Information Disclosure Statement

The information disclosure statements (IDS) submitted on 07/23/10 and 11/18/10 were filed after the mailing date of the Non-Final Office Action on 07/22/10. The submission is in compliance with the provisions of 37 CFR 1.97. Accordingly, the information disclosure statements are being considered by the examiner.

* * * * *

Terminal Disclaimer

The terminal disclaimer filed on 18 November 2010 disclaiming the terminal portion of any patent granted on this application which would extend beyond the expiration date of any patent granted on Application No. 11/078,077 has been reviewed and is accepted. The terminal disclaimer has been recorded.

* * * * *

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in Graham **v.** John Deere Co., 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later

invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 47-84 and newly added claim 85 are rejected under 35 U.S.C. 103(a) as being unpatentable over Petereit et al (hereinafter "Petereit") (U.S. Pat. Appln. Pubn. No. 2002/0160042) in view of McAllister et al. (hereinafter "McAllister") (U.S. Pat. Appln. Pubn. No. 2003/0068369).

Petereit ('042) teaches a process for producing moldings by injection-molding and injection-molded capsules made thereby, which comprise methacrylate copolymers composed of from 50% to 70% by weight of methyl acrylate, 10 to 30% by weight of methyl methacrylate, and 5% to 15% by weight of methacrylic acid (see abstract, ¶ 0005-0030 & 0038 & Example 1). The capsule may include other components, such as a release agent, a plasticizer, additives or auxiliaries, pharmaceutical agents, and other polymers or copolymers (see abstract). Plasticizers such as triethyl citrate and tributyl citrate may be included in amounts ranging up to about 30% by weight (¶ 0049-0051). Wetting agents (reads on surfactant) is disclosed on ¶ 0052. Stearyl alcohol (0.1-3%) and talc (0-50%) are also disclosed (¶ 0043-0047). Polymers such as hydroxypropyl cellulose and polyvinylpyrrolidones may be included in amounts of up to 20% by weight (¶ 0078) to [0080]). The processing of the ingredients takes place in an extruder in a temperature ranging from 120°C to 250°C (¶ 0030). In one embodiment, the mixture is processed in a twin-screw extruder, with the resulting extrudate being chopped to give pellets (¶ 0099). The molded capsules may be joined by various methods including adhesive bonding, welding by laser, ultrasound or microwaves, or by means of a snap connection (¶ 0095). In one embodiment, a capsule with a wall thickness of 0.6 mm is produced (¶ 0101). Suitable polymers

disclosed include (meth)acrylate copolymers with quaternary ammonium groups and containing trimethylammoniumethyl methacrylate chloride as monomer (Eudragit® RL and/or Eudragit® RS) (¶ 0080).

Petereit does not teach the instantly claimed amount of surfactant (of less than 2% as in claim 56); does not teach the instantly claimed amount of the lubricant stearyl alcohol (from about 10 to about 15%); does not teach absorption enhancers and does not teach a blend of hydroxypropyl cellulose polymers having a differing molecular weight.

McAllister ('369) teaches pharmaceutical polymeric compositions suitable for injection molding of single or multi-component pharmaceutical dosage forms comprising a plurality of drug substance containing sub-units, being capsule compartments and/or solid subunits comprising a solid matrix of a polymer which contains a drug substance, the sub-units being connected in the assembled dosage form by a weld between parts of the assembled dosage form (see Abstract). Also disclosed are injection-molded capsule shells, linkers, spacers, multi-component injection molded capsule shells, linkers, spacers and multicomponent dosage forms (page 1, ¶ 0007 & 0012).

Polymers suitable for injection molding include PEO, PEG, mixtures of PEO & PEG, PVA, PVP, cellulose derivatives such as hydroxypropyl cellulose, hydroxypropylmethyl cellulose (HPMC), hydroxypropylmethyl cellulose phthalate, cellulose acetate phthalate, starch and its derivatives, sodium starch glycolate, polysaccharides such as chitosan, polyacrylates and poly(meth)acrylates and its derivatives such as the Eudragit® family of polymers and combinations and mixtures thereof (p. 9, ¶ 0122).

More suitable methacrylic acid copolymers disclosed include Eudragit®RL and/or Eudragit®RS (p. 10, ¶ 0125). The copolymers can be used in amounts of 20% w/w or more (p. 10, ¶ 0127). Preferred polymers disclosed are Eudragit®RL 100. A suggested blend of polymers would be the combination of RL and RS with the necessary glidants and excipients (p. 10, ¶ 0131).

Water soluble and water-insoluble polymers are discussed at p. 10, ¶ 0136-0137.

The polymer material includes substances which modify their properties, such as: lubricants, surfactants, absorption enhancers, plasticizers, dissolution modifying agents and the like (p. 11, ¶ 0142). Specific substances are disclosed at page 11, (p. 11, ¶ 0143 - p. 12 ¶ 0156). These substances (lubricant - i.e., stearyl alcohol; surfactant; plasticizers, etc.) are the same as those claimed by Applicant. Lubricants are disclosed in amounts of from about 0 to about 30% w/w (p. 12, ¶ 0154). Surfactants are provided in amounts of from 0 to about 10% and include sodium dodecyl sulphate or block copolymers of ethylene oxide and propylene oxide (¶ 0143 & 0144). Absorption enhancers such as lecithin, sucrose fatty acid esters, Vitamin E-TPGS are also disclosed (p. 11, ¶ 0142-0143). Blends of hydroxypropyl cellulose polymers having differing molecular weight are disclosed at p. 12, ¶ 0150 and include KLUCEL. Suitable amounts of dissolution modifying agents (i.e., disintegrants) are about 10% to 40% as well as 10% to 70% for swellable solids such as hydroxypropylcellulose (p. 12, ¶ 0152). In the case where the claimed ranges "overlap or lie inside ranges disclosed by the prior art" a prima facie case of obviousness exists. In re Wertheim, 541 F.2d 257, 191 USPQ 90 (CCPA 1976); In re Woodruff, 919 F.2d 1575, 16 USPQ2d 1934 (Fed. Cir. 1990). **Newly added claim 85** recites "wherein the blend of hydroxypropyl cellulose polymers each having a differing molecular

weight is of equal % w/w". It is the position of the Examiner that in the absence of any claimed percentages, amounts or ranges, this limitation does not render a patentable distinction over the hydroxypropyl cellulose polymer blends disclosed by McCallister. Moreover, note in particular that McCallister discloses suitable and effective percentage ranges of their swellable solids (i.e., 10% to 70% of swellable solids such as hydroxypropylcellulose). (See p. 12, ¶ 0152).

Moreover, with regards to the amounts and/or ranges being claimed, it is the position of the Examiner that suitable amounts and/or ranges could be determined by one of ordinary skill in the art through routine or manipulative experimentation to obtain optimal results, as these are variable parameters attainable within the art. Moreover, generally, differences in concentration will not support the patentability of subject matter encompassed by the prior art unless there is evidence indicating such concentration is critical. "[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation." In re Aller, 220 F.2d 454, 456, 105 USPQ 233, 235 (CCPA 1955).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to include the specific ranges/amounts of surfactant and lubricant, the absorption enhancers and blends of hydroxypropyl cellulose polymers as taught by McCallister within the formulations of Petereit. One would do so with a reasonable expectation of success because McCallister teaches the use of processing agents, excipients and additives (i.e., surfactants, lubricants, absorption enhancers) in beneficially-effective amounts and ranges and further teaches blends of hydroxypropylcellulose polymers (i.e., KLUCEL) which are utilized for their dissolution modifying effects. The expected result would be an improved process for formulating injection molded compositions. Thus, the instant invention would have been prima

facie obvious to one of ordinary skill in the art, given the combined teachings of Petereit and McCallister ('369).

* * * * *

Claims 47-64, 69-77, 82 and 83 are rejected under 35 U.S.C. 103(a) as being unpatentable over Petereit et al (hereinafter "Petereit") (U.S. Pat. Appln. Pubn. No. 2002/0160042) in view of McAllister et al. (hereinafter "McAllister") (U.S. Pat. Appln. Pubn. No. 2003/0049311).

Petereit ('042) teaches a process for producing moldings by injection-molding and injection-molded capsules made thereby, which comprise methacrylate copolymers composed of from 50% to 70% by weight of methyl acrylate, 10 to 30% by weight of methyl methacrylate, and 5% to 15% by weight of methacrylic acid (see abstract, ¶ 0005-0030 & 0038 & Example 1). The capsule may include other components, such as a release agent, a plasticizer, additives or auxiliaries, pharmaceutical agents, and other polymers or copolymers (see abstract). Plasticizers such as triethyl citrate and tributyl citrate may be included in amounts ranging up to about 30% by weight (¶ 0049-0051). Wetting agents (reads on surfactant) is disclosed on ¶ 0052. Stearyl alcohol (0.1-3%) and talc (0-50%) are also disclosed (¶ 0043-0047). Polymers such as hydroxypropyl cellulose and polyvinylpyrrolidones may be included in amounts of up to 20% by weight (¶ 0078). to [0080]). The processing of the ingredients takes place in an extruder in a temperature ranging from 120°C to 250°C (¶ 0030). In one embodiment, the mixture is processed in a twin-screw extruder, with the resulting extrudate being chopped to give pellets (¶ 0099). The molded capsules may be joined by various methods including adhesive bonding, welding by laser, ultrasound or microwaves, or by means of a snap connection (¶ 0095). In one

embodiment, a capsule with a wall thickness of 0.6 mm is produced (¶ 0101). Suitable polymers disclosed include (meth)acrylate copolymers with quaternary ammonium groups and containing trimethylammoniumethyl methacrylate chloride as monomer (Eudragit® RL and/or Eudragit® RS) (¶ 0080).

Petereit does not teach the instantly claimed amount of surfactant (of less than 2% as in claim 56); does not teach the instantly claimed amount of the lubricant stearyl alcohol (from about 10 to about 15%) and does not teach absorption enhancers.

McAllister ('311) teaches pharmaceutical polymeric compositions suitable for injection molding of single or multi-component pharmaceutical dosage forms comprising a plurality of drug substance containing sub-units, being capsule compartments and/or solid subunits comprising a solid matrix of a polymer which contains a drug substance, the sub-units being connected in the assembled dosage form by a weld between parts of the assembled dosage form (see Abstract). Also disclosed are injection-molded capsule shells, linkers, spacers, multi-component injection molded capsule shells, linkers, spacers and multicomponent dosage forms (page 1, ¶ 0007 & 0012).

Polymers suitable for injection molding include PEO, PEG, mixtures of PEO & PEG, PVA, PVP, cellulose derivatives such as hydroxypropyl cellulose, hydroxypropylmethyl cellulose (HPMC), hydroxypropylmethyl cellulose phthalate, cellulose acetate phthalate, starch and its derivatives, sodium starch glycolate, polysaccharides such as chitosan, polyacrylates and poly(meth)acrylates and its derivatives such as the Eudragit® family of polymers and combinations and mixtures thereof (p. 9, ¶ 0120).

More suitable methacrylic acid copolymers disclosed include Eudragit®RL and/or Eudragit®RS (p. 10, ¶ 0123). The copolymers can be used in amounts of 20% w/w or more (p. 10, ¶ 0125). Preferred polymers disclosed are Eudragit®RL 100. A suggested blend of polymers would be the combination of RL and RS with the necessary glidants and excipients (p. 10, ¶ 0130).

Water soluble and water-insoluble polymers are discussed at p. 10, ¶ 0135-0136.

The polymer material includes substances which modify their properties, such as: lubricants, surfactants, absorption enhancers, plasticizers, dissolution modifying agents and the like (p. 11, ¶ 0141). Specific substances are disclosed at page 11, (p. 11, ¶ 0143 – p. 12 ¶ 0160). These substances (lubricant - i.e., stearyl alcohol; surfactant; plasticizers, etc.) are the same as those claimed by Applicant. Lubricants are disclosed in amounts of from about 0 to about 30% w/w (p. 12, ¶ 0155). Surfactants are provided in amounts of from 0 to about 10% and include sodium dodecyl sulphate or block copolymers of ethylene oxide and propylene oxide (¶ 0143 & 0144). Absorption enhancers such as lecithin, sucrose fatty acid esters, Vitamin E-TPGS are also disclosed (p. 11, ¶ 0141-0143). Dissolution modifying agents can comprise hydroxypropylmethyl cellulose and other hydroxyalkyl cellulose derivatives p. 11, ¶ 0146-0147. Suitable amounts of dissolution modifying agents (i.e., disintegrants, swellable solids) are from about 2.5% to 70% w/w (p. 11, ¶ 0146). In the case where the claimed ranges "overlap or lie inside ranges disclosed by the prior art" a prima facie case of obviousness exists. In re Wertheim, 541 F.2d 257, 191 USPQ 90 (CCPA 1976); In re Woodruff, 919 F.2d 1575, 16 USPQ2d 1934 (Fed. Cir. 1990).

With regards to the amounts and/or ranges being claimed, it is the position of the Examiner that suitable amounts and/or ranges could be determined by one of ordinary skill in the art through routine or manipulative experimentation to obtain optimal results, as these are variable parameters attainable within the art. Moreover, generally, differences in concentration will not support the patentability of subject matter encompassed by the prior art unless there is evidence indicating such concentration is critical. "[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation." In re Aller, 220 F.2d 454, 456, 105 USPQ 233, 235 (CCPA 1955).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to include the specific ranges/amounts of surfactant and lubricant and the absorption enhancers as taught by McCallister ('311) within the formulations of Petereit. One would do so with a reasonable expectation of success because McCallister teaches the use of processing agents, excipients and additives (i.e., surfactants, lubricants, absorption enhancers) in beneficially-effective amounts which are utilized for their superior material-effecting capabilities. The expected result would be an improved process for formulating injection molded compositions. Thus, the instant invention would have been prima facie obvious to one of ordinary skill in the art, given the combined teachings of Petereit and McCallister ('311).

* * * * *

Pertinent Art

Prior art cited of interest by the Examiner:

Clarke et al. (U.S. Patent No. 7,163,693) (01/16/2007)

Clarke discloses a multi-component pharmaceutical dosage form comprising a plurality of drug substance containing sub-units, being capsule compartments and/or solid subunits comprising a solid matrix of a polymer which contains a drug substance, the sub-units being connected in the assembled dosage form by a weld between parts of the assembled dosage form (see Abstract). Modifying agents disclosed include lubricants, surfactants, absorption enhancers, plasticizers, dissolution modifying agents and the like (col. 11, lines 20-36).

* * * * *

Response to Arguments

Applicant's arguments filed 11/18/10 have been fully considered and were found to be partially persuasive.

- **Claim Objections:**

Applicant argued, "Claims 53, 54, 63, 65-68, 77, 78 and 84 have been amended to correct minor typographical or clerical errors."

This was found persuasive, based on the amendment to the claims. Accordingly, the claim objections for claims 63 and 84 have been withdrawn.

- **Claim Rejections - 35 USC § 103(a) over Petereit ('042) in view of McCallister ('369):**

Applicant argued, "The '042 publication does not teach the specific combination of the Eudragit RL or RS polymers with the required swellable solid as a DME in the amounts as required by Claim 47 herein. The Examiner points to para. 0080 as providing for inclusion of other polymers. However, the other polymers are in fact the two copolymers which applicants start with, e.g. Eudragit RL or RS. This paragraph is specifically misleading as it includes an error. It states hydroxypropyl cellulose and then puts in brackets (HPMC). HMPC is NOT hydroxypropyl cellulose but hydroxypropylmethyl cellulose. Thus the paragraph is indefinite as

to which secondary polymer might be included. However as noted, inclusion of these polymers is in addition to the underlying (meth)acrylate copolymer Eudragit FS, Eudragit L, Eudragit NE or Eudragit S. Para 0080 does not provide for inclusion of multiple additional polymers to the first copolymer, as it does not include a statement of "combinations or mixtures thereof'. Thus to get mixture of Eudragit RL or RS and HPC is not a possible combination included within the context of the Petereit publication. More importantly, Petereit does not suggest a blend of hydroxypropylcellulose polymers having differing molecular weights, as claimed in claims 64-68. Nor does Petereit add a second dissolution modifying excipient such as claimed in claim 47 and 69."

Applicant's arguments have been considered but were not found to be persuasive. Petereit clearly teaches a process that entails the use of suitable polymers such as those disclosed at paragraph 0080. Namely, the polymers disclosed include (meth)acrylate copolymers with quaternary ammonium groups and containing trimethylammoniumethyl methacrylate chloride as monomer (Eudragit® RL and/or Eudragit® RS) (¶ 0080). The reference discloses that Eudragit® RL and/or Eudragit® RS can be used. Regarding the swellable solid as a Dissolution Modifying Excipient (DME), Petereit further teaches that polymers such as hydroxypropyl cellulose and polyvinylpyrrolidones which may be included in amounts of up to 20% by weight (¶ 0078) to [0080]) can be used. Note in particular that "mixtures" of the polymers and copolymers may be used. See (¶ 0078). Applicant points out a typographical error regarding the citation of "hydroxypropyl cellulose (HMPC)" at paragraph 0080 of Petereit. This error is noted. Applicant states that the "paragraph is indefinite as to which secondary polymer may be employed". This was not persuasive, since in any event, the disclosure of either of the HPC or HPMC would be sufficient to render the limitation of a "DME" for instant claim 47 obvious.

Applicant's argument that "inclusion of these polymers is in addition to the underlying (meth)acrylate copolymer Eudragit FS, Eudragit L, Eudragit NE or Eudragit S." and that "Para

0080 does not provide for inclusion of multiple additional polymers to the first copolymer, as it does not include a statement of "combinations or mixtures thereof" was not deemed persuasive. As delineated above, the reference teaches that "mixtures" of the polymers and copolymers may be used. See (¶ 0078). In addition, reference is also made to both Eudragit® RL **and**/or Eudragit® RS, signifying that both the RL AND RS polymers may be employed. Thus, this argument was not persuasive.

Applicant's argument that, "Petereit does not suggest a blend of hydroxypropylcellulose polymers having differing molecular weights, as claimed in claims 64-68. Nor does Petereit add a second dissolution modifying excipient such as claimed in claim 47 and 69" was not persuasive. It is noted that Petereit does not suggest a blend of hydroxypropylcellulose polymers having differing molecular weights, as claimed in claims 64-68, however, the secondary reference of McCallister was therefore invoked for the teaching that blends of hydroxypropylcellulose polymers having differing molecular weights was well known to one of ordinary skill in the art at the time the invention was made. See p. 12, ¶ 0150 of McCallister '369, whereby suitable blends disclosed include KLUCEL. Applicant's argument that "Petereit does not add a second dissolution modifying excipient such as claimed in claim 47 and 69" was not persuasive. The argument of a lack of a second dissolution modifying excipient by Petereit was unpersuasive since the current claim language does not require inclusion of a second DME. This is further evident based on the "**optionally** in combination with a second DME" claim language of instant claim 47. Thus, this argument was not held persuasive.

Regarding McCallister, '369, Applicant argued, "In contrast to the instant application, the claims and the specification of the '369 case are directed to the use of the polymer Eudragit

4135F, not the polymers Eudragit RL or RS100 as claimed herein. The Eudragit RL and RS polymers are different than that of Eudragit 4135F. The '369 specification does not disclose describe an article of manufacture having the specific composition as claimed herein. The present formulations provide for significant improvements in dissolution reproducibility".

Applicant's arguments have been considered but were not found persuasive. The McCallister '369 reference is suggestive of the teaching of the use of the polymers - Eudragit®RL and/or Eudragit®RS as claimed (p. 10, ¶ 0125). The reference is also suggestive of blends of polymers comprising a combination of RL and RS with the necessary glidants and excipients (p. 10, ¶ 0131). While the reference prefers to utilize Eudragit 4135F, the Examiner points out that disclosed examples and preferred embodiments do not constitute a teaching away from a broader disclosure or nonpreferred embodiments. In re Susi, 440 F.2d 442, 169 USPQ 423 (CCPA 1971). "A known or obvious composition does not become patentable simply because it has been described as somewhat inferior to some other product for the same use." In re Gurley, 27 F.3d 551, 554, 31 USPQ2d 1130, 1132 (Fed. Cir. 1994). In addition, whilst McCallister does not explicitly teach the claimed amounts and/or ranges, it remains the position of the Examiner suitable amounts and/or ranges could be determined by one of ordinary skill in the art through routine or manipulative experimentation to obtain optimal results, as these are variable parameters attainable within the art. Moreover, generally, differences in concentration will not support the patentability of subject matter encompassed by the prior art unless there is evidence indicating such concentration is critical. "[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation." In re Aller, 220 F.2d 454, 456, 105 USPQ 233, 235 (CCPA 1955).

Regarding Applicant's arguments directed to the need for "consistent release" and "improvements in dissolution reproducibility", these arguments were not found convincing. In this regard, the claims are entirely silent in terms of any reference to release, rates of release or dissolution profiles. Thus, Applicant's arguments are not commensurate in scope with the claims, which do not require "consistent release" as argued herein by Applicant.

- **Claim Rejections - 35 USC § 103(a) over Petereit ('042) in view of McCallister ('311):**

Applicant argued, "The '311 publication is directed to the use of the copolymer Eudragit E100 and does not disclose the inclusion of Eudragit RL or RS100 as claimed herein. The polymers in 5,705,189 are Eudragit 413F and are not Eudragit RL or RS type polymers as used herein. There is no teaching or suggestion in the US 2003/0049311 specification to direct the skilled artisan to the specific excipients and the specific % w/w amounts claimed herein to produce multicomponent dosage forms having their specific release rate characteristics. There is direction to the skilled artisan that such components would produce reliable and consistent release rates, nor what those rates would be.

The formulations disclosed in US 2003/0049311 produce capsules that dissolve at a different time frame than those of the US 2003/0068369 and to those claimed herein. The E100 components dissolve within a 17 to 34 minute window, immediately delivering the drug to the stomach contents, not as a controlled release mechanism over a longer time period, such as from 2 to 12 hours (dependent upon the additional excipients added)."

Applicant's arguments have been considered but were not found persuasive. The McCallister '311 reference is suggestive of the teaching of the use of the polymers - Eudragit®RL and/or Eudragit®RS as claimed (p. 10, ¶ 0123). The reference is also suggestive of blends of polymers comprising a combination of RL and RS with the necessary glidants and excipients (p. 10, ¶ 0130). With respect to the claimed amounts and/or ranges, as delineated

above, the determination of suitable or effective amounts is within the level of the skilled artisan. See In re Aller. Applicant argues that "McCallister (in paragraph 0123) does not teach how one formulates such a polymer to injection mold it, nor what specific excipients and amounts are necessary. This argument was not deemed convincing. Note in particular that McCallister explicitly teaches pharmaceutical polymeric compositions suitable for injection molding of single or multi-component pharmaceutical dosage forms comprising a plurality of drug substance containing sub-units, being capsule compartments and/or solid subunits comprising a solid matrix of a polymer which contains a drug substance, the sub-units being connected in the assembled dosage form by a weld between parts of the assembled dosage form (see Abstract). The reference also teaches injection-molded capsule shells, linkers, spacers, multi-component injection molded capsule shells, linkers, spacers and multicomponent dosage forms (page 1, ¶ 0007 & 0012). Thus, the reference vividly teaches injection molded formulations (i.e., capsules) as claimed. The reference further teaches use of the same components (lubricant - i.e., stearyl alcohol; surfactant; plasticizers, etc.) as that claimed by Applicant. The reference further discloses suitable amounts of dissolution modifying agents (i.e., disintegrants, swellable solids) provided in amounts of from about 2.5% to 70% w/w (p. 11, ¶ 0146). Hence, the prior art teaches injection molded capsules comprising the formulation excipients as claimed herein by Applicant. Applicant's argument that "Injection molded articles with such polymers is not the novelty of the present invention and that it is the specific formulations that provide for consistent release of the article from the mold and for use in humans as a capsule component" was not persuasive. In response to applicant's argument that the references fail to show certain features of applicant's invention, it is noted that the features upon which applicant relies (i.e., consistent

release of the article from the mold) are not recited in the rejected claim(s). Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See In re Van Geuns, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993). In this regard, the claims are entirely silent in terms of any reference to release, rates of release or dissolution profiles. Thus, Applicant's arguments are not commensurate in scope with the claims, which do not require "consistent release" as argued herein by Applicant.

- **Double Patenting:**

Applicant argued, "Application USSN 10/470,438 is directed to dosage forms comprising the copolymer 4135F, similar to that disclosed in the cited McAllister '369 publication herein.

USSN 10/470,438 and USSN 10/060849 (US 2003/0068369) are related applications to each other, but not do not teach the Eudragit RL or RS formulations as claimed herein.

The Examiner has also provisionally rejected claims 47-84 on the grounds of nonstatutory obviousness type double patenting as being unpatentable over the claims of copending application USSN 10/470,439. Applicants respectfully traverse this rejection.

Application USSN 10/470,439 is directed to dosage forms comprising the copolymer E100, similar to that disclosed in the cited McAllister US 2003/0049311 publication herein. USSN 10/470,439 and USSN 10/060,603 (US 2003/0049311) are related applications to each other, but not do not teach the Eudragit RL or RS formulations as claimed herein.

There is a copending related application USSN 11/078,077 as disclosed on Applicants 1449 forms which claims an injection molded and extruded dosage form of Eudragit RL or RS injection molded dosage forms being handled by the same Examiner. That application was filed directly in the US at 12 months, whereas the instant application is a §371 national stage entry application.

In order to advance prosecution on the merits, Applicants submit herewith a terminal disclaimer over the claims of copending application USSN 11/078,077."

These arguments have been considered and were found persuasive. Accordingly, the provisional nonstatutory obviousness-type double patenting rejections over copending Application No. 10/470,438 and copending Application No. 10/470,439 have been withdrawn in view of Applicant's persuasive remarks.

In addition, with respect to the Terminal Disclaimer filed on 11/18/10 for USSN 11/078,077, the Terminal Disclaimer has been reviewed and is accepted. The terminal disclaimer has been recorded.

Conclusion

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

--No claims are allowed at this time.

Claims 47-85 remain rejected. Claims 1-46 are cancelled.

Correspondence

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Humera N. Sheikh whose telephone number is (571) 272-0604. The examiner can normally be reached on Monday-Friday during regular business hours.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Robert A. Wax, can be reached on (571) 272-0623. The fax phone number for the organization where this application or proceeding is assigned is (571) 273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have any questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/Humera N. Sheikh/
Primary Examiner, Art Unit 1615

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January 31, 2011